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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

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05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,734	VIGH, GYULA	
	Examiner	Art Unit	
	ROBERT KASTEN	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/06/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/06/2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/06/2004, 06/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is a first non-final action on the merits.

Claims 1-35 are pending in this application.

Drawings

1. Figure 1 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 18-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Concerning Claim 18, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c).

Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989.) Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 18 recites the broad recitations "membranes" and "gels," and the claim also recites "non-ionic membranes," "isoelectric membranes," "hydrogen membranes," and "hydrogels" which are narrower statements of the above ranges/limitations. When using Markush groups, each limitation must be further limiting and non-commensurate in scope with the other members of the Markush group. The broad limitations listed above are being considered by the examiner as the genus of the narrower limitations, which are being considered species of those broad limitations. Claims 19-22 are rejected for being dependent on an indefinite claim.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5, 9-11, 14-20, 23-28 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by MARTIN et al. (US 4,243,507), from here on referred to as MARTIN, with supporting evidence provided by PENG et. al.

(*Journal of Colloid and Interface Science,* 271 (2004) 277-283), from here on referred to as PENG.

Concerning Claim 1, MARTIN teaches the separation of substances using electrophoresis by isoelectric focusing, employing a plurality of isoelectric membranes to do so (abstract, lines 1-4). Specifically, MARTIN teaches placing an ampholytic component (bovine serum albumin or BSA) having an isoelectric point, into this electrophoresis separation system (col. 8, line 2). BSA inherently has an isoelectric point. The separation system comprises appropriate electrolytes for anode and cathode, which correspond to the anolyte and a catholyte for the system (col. 5, lines 29-30) and these electrolytes inherently have pHs. The catholyte is sodium hydroxide, which has a higher pH than the anolyte, which is sulphuric acid (col. 5, lines 58-64). The separation system also comprises a plurality of isoelectric barriers with pI values (col. 5, lines 5-6) which separate buffer compartments in such a way that each isoelectric barrier has a buffer compartment with a pH lower than its own pI on its anodic side and a buffer compartment with a pH higher than its own pI on its cathodic side. The isoelectric barriers can be considered to be ion-permeable (col. 4, lines 15-29).

MARTIN also teaches the use of an isoelectric buffer with a pI equal to its pH (col. 4, lines 62-66) be different than the ampholytic sample, as is evidenced by Table II in column 8 and column 8, lines 2-4. Table II shows an array of buffer compartments 1-5 with pH values at certain times. At time 0, the pH of compartment 4 is 5.5, which greater than that of the anolyte (anolyte pH <4.0), less than that of the catholyte (catholyte pH > 6.05), and different from the pI of

the contained sample, BSA (BSA pI = 4.7). For evidence for the pI of BSA, see PENG, pg. 280, line 11. Further, the buffer has a different pI from the surrounding membranes (col. 3, line 67- col. 4, line 2).

Finally, an electric potential is supplied between the anode and the cathode (the electric field from col. 4, line 64).

Concerning Claim 2, MARTIN teaches all the limitations of claim 1. MARTIN also teaches an anode and a cathode in appropriate electrolyte baths or compartments (col. 5, lines 29-40). Further, MARTIN teaches a series of isoelectric (ion-permeable) membranes with various pIs disposed between the two baths (col. 5, lines 1-15).

Concerning Claim 3, MARTIN teaches all the limitations of claim 2. Further, MARTIN teaches a plurality of ion-permeable barriers positioned between the anode and cathode compartments (col. 5, lines 1-39). Inherently, these membranes create multiple compartments like those seen in Figure 1 of MARTIN (features 4, 6, 2s, 10, 8).

Concerning Claim 4, MARTIN teaches all the limitations of claim 3. Further, MARTIN teaches that the plurality of ion-permeable barriers are arranged by changing pI from anode to cathode (col. 5, lines 1-15).

Concerning Claim 5, MARTIN teaches all the limitations of Claim 3. Further, MARTIN teaches in col. 8, lines 2-4 that the sample can be introduced to one of the sample compartments (called circuits by MARTIN here), in this case circuit (compartment) 4.

Concerning Claim 9, MARTIN teaches all the limitations of claim 3. Further, MARTIN teaches a plurality of ion-permeable barriers, arranged by changing pI from anode to cathode (col. 5, lines 1-15), positioned between the anode and cathode compartments (col. 5, lines 1-39). These membranes create multiple compartments like those seen in Figure 1 of MARTIN (features 4, 6, 2s, 10, 8).

Concerning Claim 10, MARTIN teaches all the limitations of claim 9. Further, MARTIN teaches that the plurality of ion-permeable barriers are arranged by changing pI from anode to cathode (col. 5, lines 1-15).

Concerning Claim 11, MARTIN teaches all the limitations of claim 9. Further, MARTIN teaches in col. 8, lines 2-4 that the sample can be introduced to one of the sample compartments (called circuits by MARTIN here), in this case circuit (compartment) 4.

Concerning Claim 14, MARTIN teaches all the limitations of claim 2. Further, MARTIN teaches a plurality of ion-permeable barriers disposed between the anode and cathode compartments (col. 5, lines 1-15), which form a plurality of separation compartments (figure 1, features 4, 6, 2s, 10, 8). Finally, the ion-permeable barriers are isoelectric barriers and have different pI values (col. 5, lines 1-15).

Concerning Claim 15, MARTIN teaches all the limitations of claim 14. Further, MARTIN teaches the device have more than 2 ion-permeable, isoelectric barriers (col. 4, lines 12-14).

Concerning Claim 16, MARTIN teaches all the limitations of claim 15. Further, MARTIN teaches a plurality of ion-permeable, isoelectric barriers which have different pI values (col. 5, lines 1-15).

Concerning Claim 17, MARTIN teaches all the limitations of claim 9. Further, MARTIN teaches the presence of isoelectric buffer compartments between the isoelectric barriers (col. 6, lines 5-8), these buffer compartments having a pI different from each other (col. 3, line 67- col. 4, line 2).

Concerning Claim 18, MARTIN teaches all the limitations of Claim 1. Further, MARTIN teaches that the isoelectric barriers are isoelectric membranes (col. 5, line 6).

Concerning Claim 19, MARTIN teaches all the limitations of claim 19. Further, MARTIN teaches in claim 3 that the gel membrane is a chemically treated polyacrylamide gel. The term "gel" necessarily anticipates "hydrogel" because of their structural and functional similarities and their use in the art.

Concerning Claim 20, MARTIN teaches all the limitations of claim 18. Further, MARTIN teaches making the membranes by soaking hardened filter paper in hot aqueous agarose, thus creating a crosslinked polymer network necessarily supported by the paper (col. 6, lines 46-49). MARTIN teaches that either agarose or polyacrylamide may be used in claim 3.

Concerning Claim 23-24, MARTIN teaches all the limitations of Claim 1. Further, MARTIN teaches that the isoelectric barriers are isoelectric membranes (col. 5, line 6).

Concerning Claim 25, MARTIN teaches all the limitations of Claim 1. Further, absent any specific method claimed by applicant to avoid convective mixing, the claimed limitation must be deemed inherent to the device of MARTIN because said device anticipates all prior claimed limitations.

Concerning Claim 26, MARTIN teaches all the limitations of Claim 1. Further, MARTIN teaches the presence of isoelectric buffer compartments between the isoelectric barriers (col. 6, lines 5-8).

Concerning Claim 27, MARTIN teaches all the limitations of Claim 26. Further, MARTIN teaches in Table II that the pI values of the isoelectric buffer differ from the pI value of the sample. BSA (pI = 4.7) is placed in circuit 4 (pH=pI=5.5).

Concerning Claim 28, MARTIN teaches all the limitations of Claim 1. Further, MARTIN teaches the claimed relationship between pKa and pI in column 1, lines 58-61, specifically that the pKa be within 1 pH unit of the pI.

Concerning Claim 34-35, MARTIN teaches all the limitations of Claim 34. Further, MARTIN teaches that the sample to be separated is a protein, BSA (col. 8, line 2).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 6-8 and 12-13 rejected under 35 U.S.C. 103(a) as being unpatentable over MARTIN, with supporting evidence supplied by MOHAN et. al. (*Journal of Chromatography,* 271 (2004) 277-283), from here on referred to as MOHAN.

Concerning Claim 6-7, MARTIN teaches all the limitations of Claim 5. Further, MARTIN teaches that a sample is provided to a sample compartment (col. 8, line 2) and then separated.

MARTIN does not expressly teach that the ampholytic components of the sample are separated in a non-isoelectric state.

However, MARTIN appears to teach ampholytic component separation in a non-iso-electric state implicitly. Table II details the focusing of BSA, the ampholytic component of a sample. The pI of BSA is 4.7 according to PENG (see discussing in claim 1.) The sample starts at time 0 in a compartment with pH 5.5, but ends up having a large concentration at time 45 minutes in compartment 3, which has a pH of 5.05. Therefore, when the sample of BSA is removed, its pI will be different from the buffer's pH and therefore different from

its pI. This is consistent with the applicant's definition of a non-isoelectric state, and therefore reads on those claims.

Concerning Claim 8, MARTIN teaches all the limitations of Claim 3. Further, MARTIN teaches the separation of two ampholytic components (BSA and "horse heart cytochrome") at once.

MARTIN does not expressly teach that the ampholytic components of the sample are separated and then obtained in a non-isoelectric state.

However, MARTIN appears to teach ampholytic component separation in a non-iso-electric state implicitly. Table II details the focusing of BSA and horse heart cytochrome, the ampholytic components of a sample. The pI of BSA is 4.7 according to PENG (see discussing in claim 1.) while the pI of "horse heart cytochrome" is 10.3 (MOHAN, abstract). The sample starts at time 0 in a compartment with pH 5.5, but end up having a large concentration at time 45 minutes of BSA in compartment 3, which has a pH of 5.05, and "horse heart cytochrome" in compartment 5 (col. 8, lines 47-48), which has a pH of 6.05. Therefore, when the samples of BSA and "horse heart cytochrome" are removed, the pIs of the respective proteins will be different from the corresponding compartment's buffer pH, and therefore its pI. This is consistent with the applicant's definition of non-isoelectric state, and therefore reads on those claims.

Concerning Claims 12-13, MARTIN teaches all the limitations of claim 11. Further, MARTIN teaches the separation of two ampholytic components (BSA and "horse heart cytochrome") at once.

MARTIN does not expressly teach that the ampholytic components of the sample are separated and then obtained in a non-isoelectric state.

However, MARTIN appears to teach this implicitly. Table II details the focusing of BSA and horse heart cytochrome, the ampholytic component of a sample. The pI of BSA is 4.7 according to PENG (see discussing in claim 1.) while the pI of “horse heart cytochrome" is 10.3 (see Mohan, *Journal of Chromatography*, referenced at end of action). The sample starts at time 0 in a compartment with pH 5.5, but end up having a large concentration at time 45 minutes of BSA in compartment 3 which has a pH of 5.05, and “horse heart cytochrome" in compartment 5 (col. 8, lines 47-48), which has a pH of 6.05. Therefore, when the samples of BSA and “horse heart cytochrome" are removed, the pIs of the respective proteins will be different from the corresponding compartment’s buffer pH, and therefore its pI. This is consistent with the applicant’s definition of non-isoelectric state, and therefore reads on those claims.

9. Claims 21 and 22 rejected under 35 U.S.C. 103(a) as being unpatentable over MARTIN in view of SPEICHER et. al. (US 6,638,408), from here on referred to as SPEICHER.

Concerning Claim 21, MARTIN teaches all the limitations of claim 18.

MARTIN does not expressly teach that the ion-permeable barrier is a porous frit such as glass, ceramic, or polymeric frits.

However, SPEICHER teaches a method and device for separation of charged molecules using isoelectric focusing best exemplified by Figure 1.

Figure 1 shows the device with charged membranes (110, 120) at either end of a channel with compartments (170, 180, etc) defined by porous membranes (130-160). The device can be used to separate proteins (col. 4, line 46). Further, the porous membranes may be made of "a glass membrane filter." Examiner has construed "glass membrane filter" to read on glass frit.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to replace the gel membranes of MARTIN with the glass membrane filters of SPEICHER because the glass membrane is likely to require less maintenance than a polyacrylamide one and could be potentially reused across multiple experiments, whereas the gel membranes are likely to dry out or degrade over shorter periods of time.

Concerning Claim 22, MARTIN teaches all the limitations of Claim 18.

MARTIN does not expressly teach that the ion-permeable membranes restrict the flow of macromolecules of a certain size.

However, SPEICHER teaches that "a membrane permeable to small ions can have a molecular cut-off of, for example, at least about 1, 5, 10, or 30 kDa (col. 5, lines 44-48)."

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to have molecular weight cut-offs like in SPEICHER in the membranes MARTIN because those cut-offs allow for better control while separating substances, and could help screen for impurities and unwanted variants of a target protein within a mixed sample.

10. Claims 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over MARTIN in view of SOEDERBERG et. al. (US 4,334,972), from here on in referred to as SOEDERBERG.

Concerning Claims 29-31, MARTIN teaches all the limitations of claim 1.

MARTIN does not expressly teach that the isoelectric buffer is glutamic acid or lysine.

However, SOEDERBERG teaches an ampholytic buffer for isoelectric focusing whose primary components are glutamic acid or lysine.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use the buffer composition of SOEDERBERG in the device of MARTIN because that composition is a well established option which creates narrow ampholyte buffer pI ranges, granting the user more control during an experiment as well as more predictable results.

Concerning Claim 31, MARTIN teaches all the limitations of claim 17.

MARTIN does not expressly teach that the isoelectric buffer is glutamic acid or lysine.

However, SOEDERBERG teaches an ampholytic buffer for isoelectric focusing whose primary components are glutamic acid or lysine.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use the buffer composition of SOEDERBERG in the device of MARTIN because that composition is a well established option which creates narrow ampholyte buffer pI ranges, granting the user more control during an experiment as well as more predictable results.

11. Claims 32 and 33 rejected under 35 U.S.C. 103(a) as being unpatentable over MARTIN in view of BJELLQVIST et. al. (US 2003/0221963), from here on referred to as BJELLQVIST.

Concerning Claims 32-33, MARTIN teaches all the limitations of Claim 1.

MARTIN does not teach the use of a non-ionic detergent.

However, BJELLQVIST teaches that "it is common to include components in the separation medium that improve the solubility of the proteins and peptides to be separated. Examples of components used are well-known uncharged detergents like Triton and 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulphonate (CHAPS), but also urea is a commonly used additive. [0003]"

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use a non-ionic detergent like in BJELLQVIST in the device of MARTIN because of the disclosed advantage of improving solubility of proteins and peptides in the buffer solutions.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./
Examiner, Art Unit 1795
05/01/09

/Brian J. Sines/

Supervisory Patent Examiner, Art Unit 1795